

CLAIMS

1. A process for the preparation of 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one of formula 1, which
5 comprises hydrolyzing 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-cyclic ketal of formula 2, where:

(1) each of R₁, R₂, R₃ and R₄ is a hydrogen atom or a C₁₋₄ alkyl group, or

10 (2) R₁ and R₃ are taken together to form an alicyclic ring together with the carbon atoms in the dioxolane ring to which the groups are attached and R₂, R₄ are hydrogen atoms, or

15 (3) R₁ and R₃ are taken together to form an aromatic ring together with the carbon atoms in the dioxolane ring to which they are attached, and R₂, R₄ are taken together to form a chemical bond participating in the aromatic electron system of the aromatic ring formed by R₁ and R₃.

20 2. A process according to claim 1, which comprises hydrolyzing 3,3-ethylenedioxy-17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene.

25 3. A process according to claim 1, characterized in that 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one is obtained in a molar excess to 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one, equal at least 2:1.

4. A process according to claim 3, characterized in that 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one is obtained in a molar excess to 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one, equal at least 4:1.
- 5 5. A process according to claim 4, characterized in that 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one is obtained in a molar excess to 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one, equal at least 8:1.
6. A process according to claim 1, where the hydrolysis
10 reaction is carried out in a mixture of an organic solvent and water, in the presence of an acid having pKa value in water in the range of between 2 and 5 (pKa/H₂O= 2-5).
7. A process according to claim 1 or 6, where the acid is chosen from a group comprising oxalic acid, acetic acid,
15 fumaric acid, formic acid, malonic acid and pyridinium p-toluenesulfonate.
8. A process according to claim 7, where the acid is formic acid.
9. A process according to claim 1, characterized in that the
20 hydrolysis reaction is carried out in a mixture containing an organic solvent and water, in the presence of salts of transition metals.
10. A process according to claim 1, characterized in that the hydrolysis reaction is carried out in a mixture
25 containing an organic solvent and water, in the presence of lithium or magnesium.

11. A process according to claim 9, where the salt is copper(II) sulfate.

12. A process according to claims 1-11, characterized in that the hydrolysis reaction is carried out in a mixture of solvents containing 0%-99% water, 0%-100% of a co-solvent selected from a group consisting of THF, CHCl₃, 1,4-dioxane, CH₂Cl₂, acetone, acetonitrile, ethylmethylketone, diethylketone, 1,3-dioxolane, 1,2-dimethoxyethane, 1,2-diethoxyethane, and 0%-100% of a C₁₋₄ alcohol.

13. A process according to claims 1-12, where the reaction temperature is from about 0°C to about 200°C.

14. A process according to claims 1-13, characterized in that 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one of formula 3 is converted to a ketal of formula 2, which is then hydrolyzed to 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one.

15. A process according to claim 14, characterized in that 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one of formula 3 is converted to a 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-ketal of formula 2 by reaction with a vicinal diol, in the presence of a protic acid and a hydrocarbon solvent.

16. A process according to claim 15, characterized in that the 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-ketal of formula 2 is purified before the hydrolysis step,

by crystallization from a mixture of solvents containing 0%-50% THF, 0%-50% 1,4-dioxane, 0%-50% toluene and 0%-100% of ethyl acetate, preferably by crystallization from ethyl acetate.

5 17. 17α -Ethynyl- 17β -hydroxy- 7α -methyl-5(10)-estrene 3,3-cyclic ketal of formula 2, where

(1) each of R_1 , R_2 , R_3 and R_4 is a hydrogen atom or a C_{1-4} alkyl group, or

10 (2) R_1 and R_3 are taken together to form an alicyclic ring together with the carbon atoms in the dioxolane ring to which the groups are attached and R_2 , R_4 are hydrogen atoms, or

15 (3) R_1 and R_3 are taken together to form an aromatic ring together with the carbon atoms in the dioxolane ring to which they are attached, and R_2 , R_4 are taken together to form a chemical bond participating in the aromatic electron system of the aromatic ring formed by R_1 and R_3 .

20 18. 17α -Ethynyl- 17β -hydroxy- 7α -methyl-5(10)-estrene 3,3-cyclic ketal of formula 2, where R_1 , R_2 , R_3 , and R_4 are hydrogen atoms.

19. A compound according to claim 18, of about 90% purity.

25 20. A compound according to claim 18, of purity better than 90%.

21. A process for the preparation of pure 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-cyclic ketals of formula 2, where R₁-R₄ are defined as in claim 17, characterized in that 7 α -methyl-5(10)-estren-17-one 3,3-cyclic ketal of formula 4, where R₁-R₄ are defined as in claim 17, is reacted with a metal acetylide, in an inert solvent, while maintaining the temperature of the reaction mixture in the range from about -50°C to about +30°C.

22. A process according to claim 21, characterized in that, prior to the addition reaction, said metal acetylide is generated from acetylene gas, in the same reaction pot in which the addition to 7 α -methyl-5(10)-estren-17-one 3,3-cyclic ketal of formula 4 will subsequently be carried out.

23. A process according to claim 22, characterized in that the said reaction product of formula 2 is further purified by crystallization from a solvent containing 50-100% ethyl acetate.